

REMARKS

Claims 2-13, 19, 20, 24, 26-28, 31, 46, 48-53, and 56-58 are pending. Claims 14-18, and 55 have been withdrawn as directed to non-elected subject matter there being no allowable generic or linking claim at this time. Claim 2 has been amended to change the term “comprising” to the term “consisting essentially of.” Upon entry of this response claims 2-13, 19, 20, 24, 26-28, 31, 46, 48-53, and 56-58 are subject to examination. Now new matter has been added.

Each of the objections and rejections set forth in the Office Action are addressed below in the order presented therein.

Rejections under 35 U.S.C. § 102

Claims 2-13, 19-20, 24, 26-28, 31, 46, 48, 50, and 56-58 stand rejected under 35 USC § 102(a) and 35 U.S.C. § 102(e) as allegedly being anticipated by King (U.S. 2002/0165158 A1), as evidenced by Caplen (Trends in Biotech. 20(2):49-51, 2002). Applicants respectfully disagree.

As an initial matter, the Office stated that “with respect to claims 57-58, for the purposes of searching for and applying prior art...‘consisting essentially of’ will be construed as equivalent to ‘comprising.’”(Office Action, p. 4). Applicants respectfully refer the Office to claim 58 where the term “consisting essentially of” is not used, but rather the term “consisting” is used. As such, the rejection of claim 58 is improper because the Office has misinterpreted the claims. Accordingly, Applicants respectfully request that the rejection of claim 58 under 35 U.S.C. § 102 be withdrawn.

Claims 2-13, 19-20, 24, 26-28, 31, 46, 48, 50, and 56-58 are not anticipated by the King reference because the King reference fails to disclose a naked dsRNA molecule and King fails to disclose a method where the dsRNA is trafficked across said blood-brain or blood-retina barrier.

Applicants note that the Office’s interpretation of the term “naked” and “comprising” is incorrect. Although the Office is correct in noting that the term “comprising” is open-ended, the

interpretation of the claim must still be reasonable in view of the specification and the plain language of the claim. It is respectfully submitted that proper claim interpretation of the transition phrase provides for the recited *steps* of the method to be open-ended, but not, for example, the dsRNA molecule itself to be open-ended; particularly when such a construction directly contradicts the plain meaning of the composition. The Office alleges that the present specification states that dsRNA can be delivered with other carriers and, therefore, “naked” can be construed to include “encapsulating naked dsRNA molecules.” (Non-Final Office Action, page 6). The Office’s interpretation is incorrect and repugnant to the plain meaning and the meaning put forward in the specification. One of skill in the art would understand that the meaning of the term “naked” means that it is not encapsulated by a micelle or liposome. If a dsRNA is encapsulated, by definition it is not naked. Using the Office’s interpretation, if a claim recited “a composition comprising a naked person” that person could be reasonably interpreted to be encapsulated by clothing. If such an interpretation were used the person would no longer be naked because it would be repugnant to the definition of naked. Accordingly, the Office’s interpretation is not reasonable because it contradicts what is actually claimed.

The Office responds to the present argument regarding the interpretation of the term “naked” by referring to the specification. The Office states, citing pages 14, lines 1-5 of the present application that “the specification discloses that a preferred embodiment of the method is to administer the pharmaceutical composition comprising a naked dsRNA by suitable carrier.” Applicants respectfully refer the Office to page 14, lines 1-5 of the present application, which states:

In a preferred embodiment of the methods and uses of the present invention the composition is in a form designed to be introduced into the cells or tissue of the CNS or eye by a suitable carrier, characterized by the application occurring outside the blood-CNS and/or blood-retina barriers, for instance as eye drops. It can also be administered systemically, iontophoretically or by retrobulbar injection.

Applicants respectfully request the Office to point to where this section states that the composition comprises naked dsRNA. This embodiment does not refer to the naked dsRNA in any way that could be interpreted to include encapsulated dsRNA. There is nothing in the

present specification that permits the Office to read in the limitation that naked could encompass encapsulated by a micellar structure or liposome. The quoted portion of the specification describes an embodiment, but this embodiment is not the exclusive embodiment of the present application. The Office has taken an unreasonable interpretation of the term “naked” and compounded the mistake by reading limitations not only into the claims but also into the specification. Accordingly, the Office’s construction of the term is not reasonable.

When the proper construction of the term “naked” is used the King reference fails to anticipate the presently claimed invention. The Office responds to this argument by alleging that King discloses nucleic acids of the invention that can be combined with one or more suitable carriers that are appropriate for the route of administration and that the carrier may be saline. (Final Office Action, page 6). Although the Office does not state that these elements are equal to naked dsRNA, Applicants will interpret this rejection to mean that the combination of these elements is equivalent to the naked dsRNA that is presently claimed. Applicants respectfully assert that even viewing King in its entirety, King fails to teach or discuss a naked double-stranded oligoribonucleotides. For a reference to anticipate a claim the reference “must not only disclose all elements of the claim within the four corners of the document, but must also disclose those elements ‘arranged as in the claim.’” *NetMoney v. Verisign* 545 F.3d 1359, 1369 (Fed. Cir. 2008).

In *NetMoney*, the alleged prior art reference discloses two separate examples that contained all of the elements of the claim at issue. *Id.* at 1371. The reference, however, failed to anticipate the claim because the reference did not disclose all the elements of the claim as they were presented in the claim. *Id.* Here, the Office has done what the Federal Circuit has said is not proper for proving anticipation. The Office has picked and chosen elements from throughout the King reference in an attempt to show that the King reference discloses a naked dsRNA. The Office cannot hunt for the elements to prove that the reference discloses them in some combination. The Office must look to see what King discloses and how those elements are arranged in the claim to see if King discloses the elements in the same manner. Here, the King reference fails to disclose a naked dsRNA. Accordingly, King fails to anticipate the pending claims.

The King reference also fails to anticipate claims 8, 13, and 48. The King reference fails to discuss or suggest an inner segment of the eye ball (claim 8); a dsRNA molecule that is between 21 and 22 nucleotides in length (claim 13); or a dsRNA that contains two symmetrical 3' overhangs of two nucleotides in length (claim 48). Accordingly, the King reference cannot anticipate claims 8, 13, and 48 because the King reference fails to disclose each and every element of the claims.

For this reason and the reasons stated above, the King reference cannot anticipate the pending claims. In view of the foregoing, Applicants respectfully request that the rejection under 35 U.S.C. §102 be withdrawn.

Rejection under 35 U.S.C. § 103

Claims 2-13, 19-20, 24, 26-28, 31, 46, 48-53, and 56-58 are rejected under 35 U.S.C. §103(a), in light of Robinson et al. (U.S. Patent No. 5,814,620) in view of LaFleur et al. (U.S. Patent No. 6,433,145), and Tuschl et al. (U.S. Patent Application No. 2002/0086356). Applicants respectfully disagree.

The claims are not obvious because the combination of the references fails to yield the presently claimed invention. The combination of the references does not yield a composition comprising naked dsRNA. As discussed above, the Office's interpretation of the term "comprising" as it relates to the term "naked" is not reasonable. Applicants respectfully request that the Office reconsider its interpretation of the term "naked" in view of the foregoing. Applicants respectfully assert that the Office's interpretation is repugnant to the present specification and the plain meaning of the terms. One of skill in the art would not consider encapsulated dsRNA to be naked dsRNA. By definition, encapsulated cannot mean naked. Accordingly, the claims are not obvious because the combination does not yield the presently claimed invention.

The claims are also not obvious, even if the combination yielded the presently claimed invention, because the Office has failed to show that one of skill in the art would have had a reasonable expectation of success performing the claimed method with naked dsRNA. As

discussed previously, there is no indication that naked dsRNA can even cross the blood-brain or the blood-retina barrier. The additional references to other elements of the claims merely recite added elements, without addressing this primary deficiency. As such, the references do not teach or even suggest each and every element of the claims with a reasonable expectation of success. The Office's response to this fact is to use an unreasonable interpretation of the claims to show that the combination yields the presently claimed invention. Applicants respectfully assert that in view of a reasonable interpretation of the claims, the obviousness rejection must be withdrawn.

The Office alleges that in view of Robinson and LaFleur it was "routine for those of ordinary skill in the art to formulate a composition consisting essentially of a dsRNA molecule and saline." Applicants refer to Robinson Examples 2 and 3 and LaFleur's recitation of a naked polynucleotide. Applicants respectfully disagree with the interpretation of these references. Robinson fails disclose a dsRNA oligonucleotide. Examples 2 and 3 of Robinson describe the administration of an antisense oligonucleotide, which is a single-stranded oligonucleotide. LaFleur cannot remedy this deficiency because LaFleur also fails to disclose a naked dsRNA oligonucleotide. LaFleur discloses DNA and RNA, but not dsRNA. Single stranded RNA molecules and dsRNA molecules are not equivalents and the Office has provided no evidence as to why they would be considered equivalent by one of skill in the art. Therefore, the Office's conclusion that it was "routine" to formulate a naked dsRNA composition is not supported by the cited references. "[R]ejections on obviousness cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." (M.P.E.P. 2141, quoting *KSR v. Teleflex S Ct.* 2007). Here, the Office's conclusion of obviousness is based on facts that are not in the references. Robinson and LaFleur do not show that it was routine to use naked dsRNA. The Office has failed to cite any other reference to cure this deficiency. Accordingly, the Office has failed to carry its burden to support a finding that the claims are *prima facie* obvious because the Office has failed to demonstrate that there would have been a reasonable expectation of success based upon the cited references. Therefore, the rejection must be withdrawn.

In view of the foregoing, Applicants respectfully request that the rejection under 35 U.S.C. § 103 be withdrawn.

CONCLUSION

For the reasons discussed above, Applicants respectfully request reconsideration of the rejections of the claims. Applicants believe that the claims are in proper form for allowance. If the undersigned can be of assistance to the Examiner regarding any of the above, please contact the undersigned at the number set forth below.

It is not believed that any additional fees are due; however, in the event that an additional fee is required for this response, the Commissioner is hereby authorized to charge such fees to Deposit Account No. 50-0436.

Respectfully submitted,



By: _____

Daniel M. Scolnick, Ph.D.
Reg. No. 52,201

PEPPER HAMILTON LLP
One Mellon Center, 50th Floor
500 Grant Street
Pittsburgh, PA 15219
Phone: (412) 454-5000
Facsimile: (412) 281-0717
Date: March 4, 2010